

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
6 October 2005 (06.10.2005)

PCT

(10) International Publication Number  
**WO 2005/092929 A1**

(51) International Patent Classification<sup>7</sup>: **C08B 37/00**,  
A61K 47/48

(21) International Application Number:  
PCT/IB2005/000780

(22) International Filing Date: 25 March 2005 (25.03.2005)

(25) Filing Language: Italian

(26) Publication Language: English

(30) Priority Data:  
MI2004A000605 29 March 2004 (29.03.2004) IT

(71) Applicant (for all designated States except US): **SINTO-FARM S.P.A.** [IT/IT]; Via Togliatti 5, I-42016 Guastalla (IT).

(71) Applicant: **FERLINI, Giovanna** (heiress of the deceased inventor) [IT/IT]; Via IV Novembre 14, I-37126 Verona (IT).

(71) Applicant and

(72) Inventor: **CORADINI, Danila** [IT/IT]; Via Pecorini, 7, I-20138 Milano (IT).

(72) Inventor: **PERBELLINI, Alberto** (deceased).

(74) Agent: **GERLI, Paolo**; Notarbartolo & Gervasi S.p.A., Corso di Porta Vittoria 9, I-20122 Milan (IT).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **HYALURONIC ACID BUTYRIC ESTERS WITH A LOW DEGREE OF SUBSTITUTION, PROCEDURE FOR THEIR PREPARATION AND USE**

(57) Abstract: The invention relates to hyaluronic acid butyric esters in which the hydroxyl groups of hyaluronic acid are partially esterified with butyric residues, characterised by a degree of substitution with butyric residues (ratio of number of butyric acid residues to disaccharide units GlcNAc-GlcUA of hyaluronic acid) being equal or below 0.1. These esters with low degree of substitution are obtained by means of a process carried out in the homogeneous phase under anhydrous conditions, wherein hyaluronic acid is used in the form of a quaternary nitrogen salt. The esters of the invention have a greater antiproliferative activity than corresponding esters with higher degree of substitution, and are particularly active against primary and metastatic tumours, where said tumours are primary of hepatic origin, or are hepatic metastases. A further aspect of the invention is represented by pharmaceutical compositions, containing as active principle at least one of the esters described.



**WO 2005/092929 A1**